

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
29 January 2004 (29.01.2004)

PCT

(10) International Publication Number
WO 2004/009057 A1

(51) International Patent Classification⁷: **A61K 9/10.** (74) Agent: ASTRAZENECA; Global Intellectual Property, Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).

(21) International Application Number:
PCT/GB2003/003044

(22) International Filing Date: 14 July 2003 (14.07.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0216700.5 18 July 2002 (18.07.2002) GB

(71) Applicant (*for all designated States except MG, US*): ASTRAZENECA AB [SE/SE]; Sodertalje, S-151 85 (SE).

(71) Applicant (*for MG only*): ASTRAZENECA UK LIMITED [GB/GB]; 15 Stanhope Gate, London, Greater London W1K 1LN (GB).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): SKANTZE, Tommy, Urban [SE/SE]; AstraZeneca R & D Mölndal, S-431 83 Mölndal (SE). LINDFORS, Per, Lennart [SE/SE]; AstraZeneca R & D Mölndal, S-431 83 Mölndal (SE). FORSSEN, Sara [SE/SE]; AstraZeneca R & D Mölndal, S-431 83 Mölndal (SE).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/009057 A1

(54) Title: PROCESS FOR THE PREPARATION OF CRYSTALLINE NANO-PARTICLE DISPERSIONS

(57) Abstract: A process for the preparation of a dispersion of crystalline nano-particles in an aqueous medium comprising combining (i) a first solution comprising a substantially water-insoluble substance in a water-miscible organic solvent with; (ii) an aqueous phase comprising water and optionally a stabiliser, to form a dispersion of amorphous particles; and (iii) sonicating the dispersion of amorphous particles for a sufficient period to form crystalline nano-particles of the substantially water-insoluble substance. The process provides nano-crystals with a mean hydrodynamic diameter of less than 1 micron, particularly less than 300 nm and is particularly useful for the preparation of nano-crystalline dispersions of pharmaceutical substances.

INTERNATIONAL SEARCH REPORT

Int'l Application No
P 03/03044

A. CLASSIFICATION OF SUBJECT MATTER		
IPC 7 A61K9/10 A61K9/14 A61K9/51		
<p>According to International Patent Classification (IPC) or to both national classification and IPC</p>		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
IPC 7 A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
EPO-Internal, WPI Data, PAJ		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	US 2003/059472 A1 (DOTY MARK ET AL) 27 March 2003 (2003-03-27) claims 1-6,18,25-33,43-47,51-62; figure 1	1-14,16, 17
X	WO 99 00113 A (MAGDASSI SHLOMO ;SAHADEVAN DAVID C (US); SOON SHIONG PATRICK (US);) 7 January 1999 (1999-01-07) page 9, paragraph 2; claims 53,61,62; example 19 page 21, paragraph 2 -page 22, line 21 page 35	1-6,11, 12,14,17
X	WO 98 14174 A (SOON SHIONG PATRICK ;TAO CHUNLIN (US); YANG ANDREW (US); DESAI NEI) 9 April 1998 (1998-04-09) page 10, paragraph 3; claims 1,12,21-27,36; example 2 page 18, paragraph 2	1-5,11, 14,16,17
-/-		
<input checked="" type="checkbox"/>	Further documents are listed in the continuation of box C.	<input checked="" type="checkbox"/> Patent family members are listed in annex.
* Special categories of cited documents :		
"A" document defining the general state of the art which is not considered to be of particular relevance		
"E" earlier document but published on or after the international filing date		
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)		
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention		
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone		
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art		
"&" document member of the same patent family		
Date of the actual completion of the International search		Date of mailing of the international search report
25 November 2003		04/12/2003
Name and mailing address of the ISA		Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016		Kardas-Llorens, E

INTERNATIONAL SEARCH REPORT

In International Application No
 F., GB 03/03044

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RUCH F ET AL: "Preparation of micrometer size budesonide particles by precipitation" JOURNAL OF COLLOID AND INTERFACE SCIENCE, ACADEMIC PRESS, NEW YORK, NY, US, vol. 229, no. 1, 1 September 2000 (2000-09-01), pages 207-211, XP002253141 ISSN: 0021-9797 cited in the application 2. Experimental -----	1,3-12, 14,17
X	SJOESTROEM B ET AL: "THE FORMATION OF SUBMICRON ORGANIC PARTICLES BY PRECIPITATION IN AN EMULSION" JOURNAL OF DISPERSION SCIENCE AND TECHNOLOGY, NEW YORK, NY, US, vol. 15, no. 1, 1994, pages 89-117, XP009002392 ISSN: 0193-2691 Abstract page 95; table 1 -----	1-7,10, 12,14, 16,17
X	SJOSTROM B ET AL: "A METHOD FOR THE PREPARATION OF SUBMICRON PARTICLES OF SPARINGLY WATER-SOLUBLE DRUGS BY PRECIPITATION IN OIL-IN-WATER EMULSIONS. II: INFLUENCE OF THE EMULSIFIER, THE SOLVENT, AND THE DRUG SUBSTANCE" JOURNAL OF PHARMACEUTICAL SCIENCES, AMERICAN PHARMACEUTICAL ASSOCIATION. WASHINGTON, US, vol. 82, no. 6, 1 June 1993 (1993-06-01), pages 584-589, XP000367863 ISSN: 0022-3549 Abstract -----	1-8, 10-12, 14,16,17

INTERNATIONAL SEARCH REPORT

Information on patent family members

In	International Application No
I	iB 03/03044

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
US 2003059472	A1	27-03-2003	WO	03026611 A2	03-04-2003
WO 9900113	A	07-01-1999	US	6096331 A	01-08-2000
			AU	8266298 A	19-01-1999
			BR	9810945 A	05-02-2002
			CN	1267214 T	20-09-2000
			EP	1023050 A1	02-08-2000
			HU	0003972 A2	28-08-2001
			JP	2002507976 T	12-03-2002
			NO	996433 A	14-02-2000
			NZ	502500 A	28-03-2002
			WO	9900113 A1	07-01-1999
			US	6537579 B1	25-03-2003
			US	2003199425 A1	23-10-2003
			US	2003073642 A1	17-04-2003
			US	2003068362 A1	10-04-2003
			US	2003133955 A1	17-07-2003
			US	6506405 B1	14-01-2003
WO 9814174	A	09-04-1998	US	5916596 A	29-06-1999
			AU	718753 B2	20-04-2000
			AU	4592997 A	24-04-1998
			BR	9711856 A	06-11-2001
			CN	1237901 A	08-12-1999
			EP	0961612 A1	08-12-1999
			JP	2001501931 T	13-02-2001
			NO	991620 A	01-06-1999
			NZ	335133 A	22-12-2000
			WO	9814174 A1	09-04-1998
			US	2003068362 A1	10-04-2003
			US	2003133955 A1	17-07-2003
			US	6537579 B1	25-03-2003
			US	6506405 B1	14-01-2003
			US	6096331 A	01-08-2000